

**RESULTS** NVAf patients with thrombosis showed significantly higher sP-selectin ( $p < 0.001$ ) than did NVAf patients without thrombolism. Allele frequencies of (-2123C/G, -1817T/C) were significantly higher in NVAf patients with thrombosis than in NVAf patients without thrombosis, but Thr715Pro did not show any polymorphism.

**CONCLUSIONS** PS gene polymorphism may contribute to thrombotic risk in AF. sP-selectin was a potential risk factor for thrombolism in AF.

#### GW26-e4504

##### Sympathetic Nerve Remodeling in Hypertensive Rabbits with Left Ventricular Hypertrophy and Heart Failure

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**OBJECTIVES** Sympathetic nerve (SN) remodeling plays an important role in the development of sudden cardiac death in patients with myocardial infarction. However, little has been known about the pattern of SN remodeling in patients with hypertensive left ventricular hypertrophy (LVH) or heart failure (HF). We aimed to evaluate the role and pattern of SN remodeling in hypertensive rabbit models.

**METHODS** Hypertensive LVH (70% diameter stenosis,  $n=16$ ) and HF (90% diameter stenosis,  $n=12$ ) rabbit models were prepared through abdominal aorta constriction, and confirmed with echocardiographic and hemodynamic measurements. The rabbits in Sham group ( $n=14$ ) received the same procedure without abdominal aorta constriction. Eight weeks after the index procedure, ex vivo electrophysiological parameters were determined. The distribution patterns and densities of myocardial SN were determined with immunohistochemistry. The myocardial levels of cAMP and norepinephrine were measured using radioimmunoassay and high-performance liquid chromatography, respectively. Finally, the protein expression level of beta-ARK1 was determined with western-blot.

**RESULTS** Compared to Sham group, LVH group had a significantly shorter left ventricular effective refractory period ( $122.75 \pm 10.31$  ms vs  $95.71 \pm 16.31$  ms,  $P < 0.001$ ). Six isolated hearts (6/8) in LVH group occurred inducible ventricular tachycardia or ventricular fibrillation under program stimulation, while none (0/8) in Sham group occurred ( $P = 0.007$ ). All hearts (6/6) in HF group occurred spontaneous ventricular fibrillation, while the other two groups didn't have. Compared to Sham group, LVH and HF groups had significantly lower average SN density ( $7972.08 \pm 3238.78 \mu\text{m}^2/\text{mm}^2$  vs  $3226.44 \pm 2835.58 \mu\text{m}^2/\text{mm}^2$  vs  $4196.95 \pm 1572.53 \mu\text{m}^2/\text{mm}^2$ ,  $P < 0.001$ ), but higher heterogeneity of SN distribution ( $4144.17 \pm 2017.69 \mu\text{m}^2/\text{mm}^2$  vs  $5768.22 \pm 4582.05 \mu\text{m}^2/\text{mm}^2$  vs  $7858.17 \pm 2965.67 \mu\text{m}^2/\text{mm}^2$ ,  $P < 0.001$ ). The myocardial levels of cAMP ( $7.94 \pm 6.37$  ng/g vs  $20.60 \pm 7.53$  ng/g,  $p < 0.001$ ) and norepinephrine were significantly lower in the failing hearts than did those in Sham group. Meanwhile, the LVH had comparable levels of cAMP and norepinephrine as compared with Sham group. In addition, HF group rather than LVH group showed significantly lower levels of beta-ARK1 expression compared to Sham group ( $P < 0.001$ ).

**CONCLUSIONS** The present study suggests that both hypertensive LVH and HF would increase the heterogeneity of myocardial SN distributions with decreased overall SN activities, which could be translated into more vulnerable electrophysiological characteristics.

#### GW26-e4558

##### Microarray expression profile of long non-coding RNAs in human endothelial cells exposed to atheroprotective shear stress

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**OBJECTIVES** To identify differentially expressed long non-coding RNAs (lncRNAs) involved in flow-dependent regulation of vascular function.

**METHODS** Confluent human umbilical vein endothelial cells (HUVECs) were cultured under static conditions or high shear stress (HSS,  $15 \text{ dyn/cm}^2$ ) for 24 hours. Total RNA was isolated from 4 pairs of static control and shear-stressed HUVECs, and hybridized to arraystar human lncRNA 8 x 60 k v3.0 chips containing probes representing 30,586 lncRNA genes and 26,109 protein coding genes. Quantitative real-time polymerase chain reaction (RT-qPCR) was used to validate the microarray results. Bioinformatics analyses including lncRNA classification and subgroup analysis, gene ontology (GO) analysis and pathway analysis were performed.

**RESULTS** Our data revealed that 8450 out of 30,586 lncRNAs and 11,284 of 26,109 mRNAs examined were significantly altered in their expression levels at a significance level of  $P < 0.05$ . Using the cutoff criteria of P-values  $< 0.05$  and fold changes  $> 2$ , we identified 804 differentially expressed lncRNAs and 750 differentially expressed mRNAs. We confirmed the induction of one the most prominent lncRNAs CYP1B1-AS1 by HSS by RT-qPCR. 14 lncRNAs were identified as potential enhancers. GO analysis showed that the highest enriched GOs targeted by up-regulated transcripts were cell migration and the highest enriched GOs targeted by the down-regulated transcripts were mitotic nuclear division. Comparison of differentially expressed transcripts between the groups identified 11 pathways that corresponded to down-regulated transcripts and 20 pathways that corresponded to up-regulated transcripts ( $p$  value cut-off 0.05).

**CONCLUSIONS** Our results show significantly altered expression profile of lncRNAs between the static control and shear-stressed HUVECs, indicating that lncRNAs may play important roles in regulating the functions of vascular endothelial cells. Further studies should be conducted to determine the roles of these lncRNAs in flow-dependent regulation of vascular function.

#### GW26-e4592

##### Implication of C1q/TNF-related protein-12 (CTRP-12) in patients with coronary artery disease

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**OBJECTIVES** C1q/TNF-related protein-12 (CTRP-12), an adiponectin paralogue, was recently identified as novel adipokines with metabolic regulatory properties. We analyzed the relationship between CTRP-12 and coronary artery disease (CAD).

**METHODS** Subjects ( $n=188$ ,  $67 \pm 10$  years, 79% male) suspected of having CAD were enrolled in the study and were divided into two groups, CAD and non-CAD subjects, according to the results of their coronary angiographies. Serum CTRP-12 levels of the subjects were measured by an enzyme-linked immunosorbent assay.

**RESULTS** Subjects with CAD had significantly lower circulating CTRP-12 concentrations compared to the non-CAD subjects (median [interquartile range]:  $46.5$  [26.6] vs.  $53.5$  [29.6] ng/mL, respectively;  $p = 0.01$ ). The serum CTRP-12 levels significantly correlated with body mass index, the homeostasis model of assessment of insulin resistance, adiponectin levels, and CAD severity. Multivariate logistic regression analysis revealed that a decreased serum CTRP-12 level (log transformed) was independently associated with CAD for all subjects.

**CONCLUSIONS** Serum CTRP-12 levels are significantly associated with CAD in humans, suggesting that low CTRP-12 levels may contribute to CAD.

#### GW26-e4726

##### Sestrin isoform expression in the normal and failing hearts

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**OBJECTIVES** Oxidative stress and AMP-dependent protein kinase (AMPK)/mammalian target of rapamycin (mTOR) signaling pathway were closely involved in the development of cardiac hypertrophy and heart failure (HF). Previous study indicated that the Sestrin family suppressed oxidative stress and regulated AMPK / mTOR signaling. However, the expression and functions of Sestrin in hypertrophic and failing hearts are still unclear.

**METHODS** We performed quantitative RT-PCR to detect the mRNA expression of Sestrin family in the normal, hypertrophic (2 week after surgery:  $n = 4$ , 4 week after surgery:  $n = 4$ ) and failing (more than 8 week after surgery:  $n = 4$ ) mouse hearts induced by aortic banding